REMARKS

Claims 1-8 and 10-15 are pending in the present application. Claim 9 has been canceled without prejudice or disclaimer. Claims 1-8 and 10-15 have been amended.

Claim 1 has been amended to recite the following:

> An inclusion complex consisting of a reaction product of element A reacted with element B in a solvent consisting essentially of an aliphatic alcohol, wherein element A is chosen from pantoprazole, a salt of pantoprazole with a base, an enantiomer of pantoprazole, a salt of an enantiomer of pantoprazole, pantoprazole sodium sesquihydrate (= pantoprazole sodium x 1.5 H_2O), (-)-pantoprazole sodium sequihydrate, pantoprazole magnesium dihydrate, or a mixture of any two or more thereof; and wherein element B is chosen from cyclodextrin, a hydrate of cyclodextrin, a hydroxyalkyl derivative of cyclodextrin, an alkyl derivative of cyclodextrin, or a mixture of any two or more thereof.

Support for claim 1 as amended appears in the present specification at page 2, paragraph 4; the Example at page 4; and in claims 1, 2, 3, and 6 as originally filed. No new matter has been added.

Claims 4, 12 and 13, have been amended to recite a solvent consisting essentially of an aliphatic alcohol. Support for amended claims 4, 12 and 13 appears in the present specification at page 2, lines 27-28. Claim 12 has been amended to be dependent on claim 11. Claims 2-8 and 10-15 have been amended to place them in proper US form. No new matter has been added.

In view of the following, further and favorable consideration is respectfully requested.

I. At page 2 of the Official Action, claims 1, 3-8, 10-13, and 15, have been rejected under 35 USC § 112, first paragraph.

The Examiner asserts that the specification while being enabling for the free base of pantoprazole, their anhydrous salts, the sodium sesquihydrate and the magnesium dihydrate, does not reasonably provide enablement for the full scope of hydrates and solvates claimed.

In view of the following, this rejection is respectfully traversed.

Applicants assert that the specification enables the full scope of the claims including hydrates and solvates. However, in the interest of advancing prosecution of this case, claim 1 has been amended as discussed above to delete solvates and hydrates and to add the compounds recited in claim 2. Claims 3-8, 10-13, and 15, are each directly or indirectly dependent on independent claim 1.

In view of the foregoing, it is submitted that claims 1, 3-8, 10-13, and 15, fully comply with the enablement requirement of 35 USC § 112, first paragraph. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

II. At page 4 of the Official Action, claims 1, 4-8, 10, 12, 13, and 15, have been rejected under 35 USC § 103(a) as being unpatentable over Ishiguro et al.

The Examiner asserts that it would have been obvious to the skilled artisan to prepare a pantoprazole:cyclodextrin complex by substituting pantoprazole for lansoprazole in any of the examples disclosed by Ishiguro.

In view of the following, this rejection is respectfully traversed.

Claim 1 has been amended as discussed above to replace the term "a derivative of cyclodextrin" with the term "a hydroxyalkyl derivative of cyclodextrin, an alkyl derivative of cyclodextrin."

Ishiguro et al. describes a stabilized composition comprising an antiulcerative benzimidazole compound and a branched cyclodextrin-carboxylic acid. Ishiguro et al. requires the use of a branched cyclodextrin-carboxylic acid. Ishiguro et al. does not teach or suggest the use of cyclodextrin, a hydrate of cyclodextrin, a hydroxyalkyl derivative of cyclodextrin, an alkyl derivative of cyclodextrin, or a mixture of any two or more thereof, as claimed in present claim 1.

In view of the foregoing, Applicants submit that Ishiguro et al. does not teach or suggest the subject matter of present claims 1, 4-8, 10, 12, 13, and 15, within the meaning of 35 USC § 103(a). Accordingly, the Examiner is respectfully requested to withdraw this rejection.

III. At page 5 of the Official Action, claims 1, 2, 4-8, 10, and 12 -15, have been rejected under 35 USC § 103(a) as being unpatentable over Ishiguro et al. in view of Kohl.

The Examiner asserts that it would have been obvious to the skilled artisan to use any known salt form of the benzimidazole species, such as pantoprazole, for the preparation of cyclodextrin inclusion complexes with a reasonable expectation of success for their art-disclosed utility. The Examiner asserts that Kohl teaches that several salt hydrates of pantoprazole are known.

In view of the following, this rejection is moot.

As discussed above, Ishiguro et al. does not teach or suggest the use of cyclodextrin, a hydrate of cyclodextrin, a hydroxyalkyl derivative of cyclodextrin, an alkyl derivative of cyclodextrin, or a mixture of any two or more thereof, as claimed in present claim 1.

Kohl does not cure the deficiencies of Ishiguro et al. because Kohl also does not teach or suggest the use of cyclodextrin, a hydrate of cyclodextrin, a hydroxyalkyl derivative of cyclodextrin, an alkyl derivative of cyclodextrin, or a mixture of any two or more thereof, as claimed in present claim 1.

In view of the foregoing, Applicants submit that nothing in Ishiguro et al. and Kohl, taken alone or together, renders the subject matter of claims 1, 2, 4-8, 10, and 12 -15, obvious within the meaning of 35 USC § 103(a). Accordingly, the Examiner is respectfully requested to withdraw this rejection.

III. At page 5 of the Official Action, claims 1, 2, 4-8, 10, and 12 -15, have been rejected under 35 USC § 103(a) as being unpatentable over Klokkers et al.

The Examiner asserts that it would have been obvious to the skilled artisan to prepare a pantoprazole:cyclodextrin complex by substituting pantoprazole for omeprazole in any of the examples disclosed by Klokkers.

In view of the following, this rejection is respectfully traversed.

Klokkers et al. describes a pharmaceutical formulation comprising or consisting of a benzimidazole derivative, at least one cyclodextrin and at least one amino acid produced by wet-kneading.

Present claim 1 recites an inclusion complex consisting of a reaction product of element A reacted with element B in a solvent consisting essentially of an aliphatic alcohol, wherein element A is chosen from pantoprazole, a salt of pantoprazole with a base, an enantiomer of pantoprazole, a salt of an enantiomer of pantoprazole, pantoprazole sodium sesquihydrate (= pantoprazole sodium x 1.5 H_2O), (-)-pantoprazole sodium sequihydrate, pantoprazole magnesium dihydrate, or a mixture of any two or more thereof; and wherein element B is chosen from cyclodextrin, a hydrate of cyclodextrin, a hydroxyalkyl derivative of cyclodextrin, an alkyl derivative of cyclodextrin, or a mixture of any two or more thereof.

Applicant's submit that Klokkers et al. do not teach or suggest an inclusion complex consisting of a reaction product of element A reacted with element B in a solvent consisting essentially of an aliphatic alcohol, as claimed in present claim 1.

Klokkers et al. does not achieve an inclusion complex. Applicants note that Klokkers et al. states at page 4 that the main object of the invention is to guarantee a stabilization of benzimidazoles such as omeprazole as active ingredient by forming a benzimidazole/cyclodextrin inclusion complex; however, the methods described by the Klokkers reference are inoperative. Specifically, the wet-kneading method described at page 7 of Klokkers does not result in the formation of an inclusion complex.

The present specification at pages 5-11 compares different methods of preparing pantoprazole inclusion complexes. As can be seen from the data,

inclusion complexation was not achieved through wet-kneading. Specifically, as described on page 10 of the specification, differential scanning calorimetry was first used to characterize both the physical mixtures and the solid phases obtained after wetting and kneading. In none of the cases was an inclusion complex achieved by wet-kneading. Applicant's note that the Klokkers et al. reference does not describe performing any complexation studies on the compositions obtained in the Examples.

Further, Klokkers et al. requires at least one amino acid. Present claim 1 recites the transition language "consisting of." Accordingly, present claim 1 excludes all elements other than the expressly recited elements, i.e., present claim 1 does not encompass an amino acid.

Klokkers et al. describes that the at least one amino acid is required because "without an amino acid [the omeprazole/cyclodextrin inclusion complex] is not stable enough." *See* Klokkers et al. at page 4, paragraph 2. Klokkers et al. goes on to state in paragraphs 5-6 on page 4, that the main object of the invention is to guarantee a stabilization of benzimidazoles such as omeprazole as active ingredient by forming a benzimidazole/cyclodextrin inclusion complex and that the object is accomplished by complexing omeprazole with cyclodextrin in the presence of an amino acid.

Present claim 1 recites an inclusion complex consisting of a reaction product of element A reacted with element B in a solvent consisting essentially of an aliphatic alcohol. Klokkers et al. does not teach or suggest a reaction product of element A reacted with element B in a solvent consisting essentially of an

aliphatic alcohol, as claimed in present claim 1. Rather, Klokkers et al. describes a product produced by wet-kneading.

With regard to present claims 4-6 and 12-13, which recite "reacting in a solvent consisting essentially of an aliphatic alcohol" (claims 4, 6, and 12-13), and "ethanol" (claim 5), Klokkers et al. ***teaches away*** from reacting in ethanol and specifically requires wet kneading in water or ammonia water. Klokkers et al. at page 3, paragraph 4 teaches that reacting in 96% ethanol at elevated temperature results in "there is hardly active ingredient remained in the isolated product." Klokkers et al. goes on to state that "It is generally known, that ethanol is a competing cyclodextrin-complex forming agent and that from a 96% ethanolic system only the crystalline etha-nol/β-CD complex can be isolated" using the method. Accordingly, Klokkers et al. does not teach or suggest the subject matter of claims 4-6 and 12-13.

With regard to present claim 7 which recites a 1:1 inclusion complex, Klokkers et al. does not teach or suggest a 1:1 inclusion complex. To the contrary, Klokkers et al. teaches a 1:10 inclusion complex and a 1:2 inclusion complex. *See* Klokkers et al. at page 5, lines 24-25.

In view of the foregoing, it is submitted that nothing in Klokkers et al. renders the subject matter of claims 1, 2, 4-8, 10, and 12 -15, obvious within the meaning of 35 USC § 103(a). Accordingly, the Examiner is respectfully requested to withdraw this rejection.

IV. At page 6 of the Official Action, claims 1, 2, 4-8, 10, and 12 -15, have been rejected under 35 USC § 103(a) as being unpatentable over Min et al. in view of Ishiguro et al. and Kohl.

The Examiner asserts that it would have been obvious to the skilled artisan to prepare a cyclodextrin inclusion complex comprising any available salt of a benzimidazole derivative for the art-disclosed advantages of enhanced dissolution, etc.

In view of the following, this rejection is respectfully traversed.

Claim 1 has been amended to recite the following: "An inclusion complex consisting of a reaction product of element A reacted with element B in a solvent consisting essentially of an aliphatic alcohol...."

Min et al. describes reacting a benzimidazole derivative of formula (I) (which formula (I) encompasses omeprazole and lansoprazole but not pantoprazole) with cyclodextrin in an ***alkaline solution*** to produce an inclusion complex that does not include the alkaline components. Min et al. ***teaches away*** from reacting in an organic solvent such as ethanol.

Specifically, Min et al. in the paragraph bridging pages 1 and 2, describes that the process of mixing and reacting in 96% ethanol results in a discolored and degraded product. In addition, Min et al. states that using the foregoing process formation of an inclusion compound is not expected. *See also* Comparative Example 1 at page 26.

Ishiguro et al. and Kohl are discussed above.

It is submitted that none of Min et al., Ishiguro et al., and Kohl, taken alone or together, teach or suggest the inclusion complex as claimed in present claim 1, within the meaning of 35 USC § 103. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

Conclusion

In view of the foregoing, Applicant submits that the application is in condition for immediate allowance. Early notice to that effect is earnestly solicited. The Examiner is invited to contact the undersigned attorney if it is believed that such contact will expedite the prosecution of the application.

In the event this paper is not timely filed, Applicant petitions for an appropriate extension of time. Please charge any fee deficiency or credit any overpayment to Deposit Account No. 14-0112.

Respectfully submitted,

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